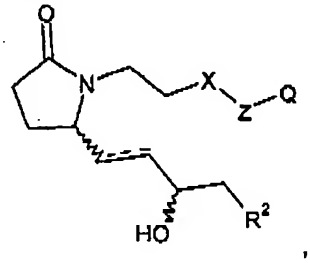
Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in this application:

Listing of Claims

1. (Amended) A compound of the formula I



I

a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein:

the dotted line is a bond or no bond;

X is $-CH_2-$ or O;

Z is $-(CH_2)_3-$, thienyl, thiazolyl or phenyl, provided that when X is O, then Z is phenyl, ~~further provided that when R^2 is selected from the group consisting of α-thienyl, phenyl, and monosubstituted phenyl, wherein said substituents being selected from the group consisting of chloro, fluoro, phenyl, methoxy, trifluoromethyl and C_1-C_3 alkyl, then Z is thienyl, thiazolyl or phenyl~~;

Q is carboxyl, $(C_1$-$C_4)$alkoxylcarbonyl or tetrazolyl;

R^2 is -Ar or $-Ar^1-V-Ar^2$;

V is a bond, -O-, -OCH_2- or -CH_2O-;

Ar is a partially saturated, fully saturated or fully unsaturated five to eight membered ring optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused independently partially saturated, fully saturated or fully unsaturated five or six membered rings, taken independently, optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen, said partially or fully saturated ring or bicyclic ring optionally having one or two oxo groups substituted on carbon or one or two oxo groups substituted on sulfur; and

Ar^1 and Ar^2 are each independently a partially saturated, fully saturated or fully unsaturated five to eight membered ring optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen, said partially or fully saturated ring optionally having one or two oxo groups substituted on carbon or one or two oxo groups substituted on sulfur;

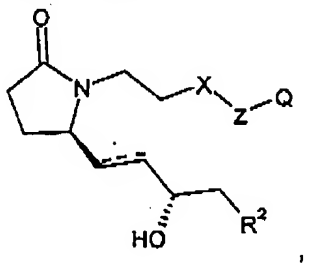
said Ar moiety is optionally substituted on carbon or nitrogen, on one ring if the moiety is monocyclic, or on one or both rings if the moiety is bicyclic, with up to three substituents per ring each independently selected from hydroxy, halo, carboxy, (C_1-C_7)alkoxy, (C_1-C_4)alkoxy(C_1-C_4)alkyl, (C_1-C_7)alkyl, (C_2-C_7)alkenyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_4)alkyl, (C_3-C_7)cycloalkyl(C_1-C_4)alkanoyl, formyl, (C_1-C_8)alkanoyl, (C_1-C_8)alkanoyl(C_1-C_8)alkyl, (C_1-C_4)alkanoylamino, (C_1-C_4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C_1-C_4)alkyl substituted aminocarbonylamino, sulfonamido, (C_1-C_4)alkylsulfonamido, amino, mono-N- or di-N,N-(C_1-C_4)alkylamino, carbamoyl, mono-N- or di-N,N-(C_1-C_4)alkylcarbamoyl, cyano, thiol, (C_1-C_6)alkylthio, (C_1-C_6)alkylsulfinyl, (C_1-C_4)alkylsulfonyl and mono-N- or di-N,N-(C_1-C_4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar are optionally substituted on carbon with up to three fluoro; and

said Ar^1 and Ar^2 moieties are independently optionally substituted on carbon or nitrogen with up to three substituents each independently selected from hydroxy, halo, carboxy, (C_1-C_7)alkoxy, (C_1-C_4)alkoxy(C_1-C_4)alkyl, (C_1-C_7)alkyl, (C_2-C_7)alkenyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_4)alkyl, (C_3-C_7)cycloalkyl(C_1-C_4)alkanoyl, formyl, (C_1-C_8)alkanoyl,

$(C_1$-$C_6)$alkanoyl$(C_1$-$C_6)$alkyl, $(C_1$-$C_4)$alkanoylamino, $(C_1$-$C_4)$alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-$(C_1$-$C_4)$alkyl substituted aminocarbonylamino, sulfonamido, $(C_1$-$C_4)$alkylsulfonamido, amino, mono-N- or di-N,N-$(C_1$-$C_4)$alkylamino, carbamoyl, mono-N- or di-N,N-$(C_1$-$C_4)$alkylcarbamoyl, cyano, thiol, $(C_1$-$C_6)$alkylthio, $(C_1$-$C_6)$alkylsulfinyl, $(C_1$-$C_4)$alkylsulfonyl and mono-N- or di-N,N-$(C_1$-$C_4)$alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar^1 and Ar^2 are optionally substituted on carbon with up to three fluoro;

provided that (a) when X is (CH_2)- and Z is $-(CH_2)_3$-, then R^2 is not thienyl, phenyl or phenyl monosubstituted with chloro, fluoro, phenyl, methoxy, trifluoromethyl or $(C_1$-$C_4)$alkyl; and (b) when X is (CH_2)-, Z is $-(CH_2)_3$-, and Q is carboxyl or $(C_1$-$C_4)$alkoxycarbonyl, then R^2 is not (i) $(C_5$-$C_7)$cycloalkyl or (ii) phenyl, thienyl or furyl each of which may be optionally monosubstituted or disubstituted by one or two substituents selected, independently in the latter case, from halogen atoms, alkyl groups having 1 - 3 carbon atoms which may be substituted by one or more halogen atoms, and alkoxy groups having 1 - 4 carbon atoms.

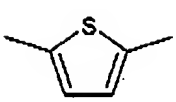
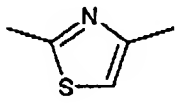
2. (Original) A compound of claim 1 of the formula Ia



Ia

a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein:

X is $-CH_2$-; Z is $-(CH_2)_3$-,

or 

and R^2 is Ar wherein said Ar moiety is optionally substituted on carbon or nitrogen, on one ring if the moiety is monocyclic, or on one or both rings if the moiety is bicyclic, with up to three substituents per ring each independently selected from hydroxy, halo, carboxy, (C_1-C_7)alkoxy, (C_1-C_4)alkoxy(C_1-C_4)alkyl, (C_1-C_7)alkyl, (C_2-C_7)alkenyl, (C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkyl(C_1-C_4)alkyl, (C_3-C_7)cycloalkyl(C_1-C_4)alkanoyl, formyl, (C_1-C_8)alkanoyl, (C_1-C_6)alkanoyl(C_1-C_6)alkyl, (C_1-C_4)alkanoylamino, (C_1-C_4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C_1-C_4)alkyl substituted aminocarbonylamino, sulfonamido, (C_1-C_4)alkylsulfonamido, amino, mono-N- or di-N,N-(C_1-C_4)alkylamino, carbamoyl, mono-N- or di-N,N-(C_1-C_4)alkylcarbamoyl, cyano, thiol, (C_1-C_6)alkylthio, (C_1-C_6)alkylsulfinyl, (C_1-C_4)alkylsulfonyl and mono-N- or di-N,N-(C_1-C_4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar^1 and Ar^2 are optionally substituted on carbon with up to three fluoro.

3. (Original) A compound of claim 2, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein Ar is cyclohexyl, 1,3-benzodioxolyl, thienyl, naphthyl or phenyl optionally substituted with one or two (C_1-C_4)alkyl, (C_1-C_4)alkoxy, (C_1-C_4)alkoxy(C_1-C_4)alkyl, chloro, fluoro, trifluoromethyl or cyano, wherein said alkyl and alkoxy substituents in the definition of Ar are optionally substituted with up to three fluoro.

4. (Original) A compound of claim 3, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein the dotted line is no bond; Q is carboxy or (C_1-C_4)alkoxylcarbonyl; and Z is

5. (Original) A compound of claim 4, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein Q is carboxy and Ar is phenyl optionally substituted with one $(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy, $(C_1$-$C_4)$alkoxy$(C_1$-$C_4)$alkyl, chloro, fluoro, trifluoromethyl or cyano, wherein said alkyl and alkoxy substituents in the definition of Ar are optionally substituted with up to three fluoro.

6. (Original) A compound of claim 5, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein Ar is m-trifluoromethylphenyl.

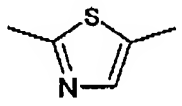
7. (Original) A compound of claim 5, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein Ar is m-chlorophenyl.

8. (Original) A compound of claim 5, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein Ar is m-trifluoromethoxyphenyl.

9. (Original) A compound selected from 5-(3-(2S-(3R-hydroxy-4-(3-trifluoromethyl-phenyl)-butyl)-5-oxo-pyrrolidin-1-yl)-propyl)-thiophene-2-carboxylic acid; 5-(3-(2S-(3R-hydroxy-4-(3-trifluoromethoxy-phenyl)-butyl)--5-oxo-pyrrolidin-1-yl)-propyl)-thiophene-2-carboxylic acid; and 5-(3-(2S-(4-(3-chloro-phenyl)-3R-hydroxy-butyl)-5-oxo-pyrrolidin-1-yl)-propyl)-thiophene-2-carboxylic acid.

10. (Original) A compound of claim 2, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein X is $-CH_2-$, Z is $-(CH_2)_3-$, Q is carboxyl or $(C_1$-$C_4)$alkoxycarbonyl and Ar is phenyl independently substituted with one to three cyano, $(C_1$-$C_7)$alkoxy substituted with one to three fluoro or $(C_1$-$C_4)$alkoxy$(C_1$-$C_4)$alkyl.

11. (Original) A compound of claim 3, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein the dotted line is no bond; Q is carboxy or (C_1-C_4)alkoxylcarbonyl; and Z is



or

12. (Original) A compound of claim 11, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein Q is carboxy and Ar is phenyl optionally substituted with one (C_1-C_4)alkyl, (C_1-C_4)alkoxy, (C_1-C_4)alkoxy(C_1-C_4)alkyl, chloro, fluoro, trifluoromethyl or cyano, wherein said alkyl and alkoxy substituents in the definition of Ar are optionally substituted with up to three fluoro.

13. (Original) A method of treating a condition which presents with low bone mass in a mammal comprising administering to said mammal a compound of claim 1, a prodrug thereof or a pharmaceutically acceptable salt of said compound or of said prodrug, or a diastereomeric mixture of said compound, salt or prodrug.

14. (Original) A method of claim 13 wherein said condition is osteoporosis, frailty, an osteoporotic fracture, a bone defect, childhood idiopathic bone loss, alveolar bone loss, mandibular bone loss, bone fracture, osteotomy, bone loss associated with periodontitis, or prosthetic ingrowth.

15. (Original) A method of claim 14 wherein said composition is administered systemically.

16. (Original) A method of claim 14 wherein said composition is administered locally.

17. (Original) A method of claim 14 wherein said condition is frailty.

18. (Original) A method of claim 14 wherein said condition is osteoporosis.

19. (Original) A method of claim 14 wherein said condition is bone fracture or osteoporotic fracture.

20. (Original) A pharmaceutical composition comprising a compound of claim 1, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt, wherein and a pharmaceutically acceptable carrier, vehicle or diluent.

21. (Original) A method of treating a condition which presents with low bone mass in a mammal comprising administering to said mammal a pharmaceutical composition of claim 20.